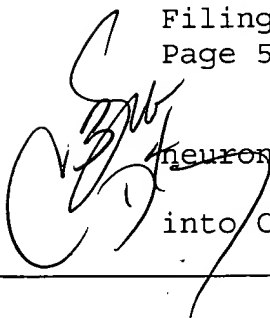


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neuron-restricted precursor cells requires FGF and differentiates into CNS neuronal cells but not into CNS glial cells.

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#### REMARKS

Claims 12, 15, 16, 21, 23, 24, 26-33, 44 and 59 are pending in the instant application. Claims 12, 15, 16, 21, 23, 24, 26-33, 44 and 59 have been rejected. Claims 12, 21, and 59 have been amended. Claim 44 has been canceled. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### I. Rejection of Claim 59 under 35 U.S.C. § 112, first paragraph

The rejection of claim 59 under 35 U.S.C. § 112, first paragraph, has been maintained. The Examiner suggests that for a population of cells to be defined as embryonic stem cells, establishment that the embryonic stem cells retain their totipotential capacity and are able to generate cells of all lineages, including germline, after being introduced into a host blastocyte, is necessary. The Examiner suggests that neither the specification nor the prior art references by Thompson et al. demonstrate this.

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While Applicants believe that the human ES cells could clearly be made and used by one skilled in the art as recited in the instant invention and commensurate in scope with claim 59, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 59 to remove the recitation of human ES cells from the claim. No new matter is added by this amendment. Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

**II. Rejection of Claims 12, 15, 16 and 26 under 35 U.S.C. § 112, second paragraph**

Claims 12, 15, 16, 21, 23, 24, 26-33, 44 and 59 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner suggests that claims 12, 21, 26 and 27 are vague and indefinite for the phrase "fail to proliferate or differentiate in astrocyte-promoting media" because it is unclear if the neuron-restricted precursor cells fail to differentiate into CNS neuronal cells or if the neuron restricted precursor cells fail to differentiate into a different cell type.

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Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended these claims to clarify that the neuron-restricted precursor cells fail to differentiate into CNS glial cells. Support for this amendment can be found throughout the specification and particularly at page 31, lines 18-21; page 33 lines 19-34; and page 37, lines 8-12. No new matter is added by this amendment.

The Examiner also suggests that claims 12, 21, 26, 27 and 59 are rendered vague and indefinite as the claims appear to be incomplete as written. The Examiner suggests that the preamble of the claims requires isolation of a pure population of cells, however, the last step recited is incubation of a subpopulation of cells.

Claims 12, 21 and 59 have been amended to clarify that the pure population of neuron-restricted cells is isolated in step (e) of claims 12 and 21; and in step (d) of claim 59, as supported throughout the specification and particularly at page 31, lines 14-17. No new matter is added by this amendment.

The Examiner suggests that claim 44 is rendered vague and indefinite in use of the phrase "derivatives thereof" as it is suggested to be unclear what type of derivation of the neuron-restricted precursor cells are required. Further, the Examiner

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suggests that it is unclear what is meant by the phrase "neurological activity" and that it is unclear what type of reaction is monitored and how the monitoring is practiced. While Applicants believe that this claim is clear in its meaning, in an earnest effort to advance the prosecution of this case, Applicants have canceled claim 44.

Withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested in light of these remarks and amendments.

### **III. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited. Attached hereto is a marked-up version of the changes made to the specification and claims by

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the current amendment. The attached page is captioned "Version with Markings to Show Changes Made".

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Kathleen A. Tyrrell".

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Registration No. 38,350

Date: March 28, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claim 44 has been canceled.

The claims have been amended as follows:

12. (Thrice amended) A method of isolating a pure population of rodent or human CNS neuron-restricted precursor cells comprising the steps of:

(a) isolating a population of rodent or human multipotent CNS stem cells which generate both neurons and glia;

(b) incubating the multipotent CNS stem cells in NEP medium;

(c) replating the multipotent CNS stem cells on laminin in the absence of chick embryo extract to induce cell differentiation;

(d) purifying from the differentiating cells a subpopulation of cells expressing embryonic neural cell adhesion molecules via a procedure selected from the group consisting of specific antibody capture, fluorescence activated cell sorting, and magnetic bead capture; and

(e) isolating a pure population of rodent or human CNS neuron-restricted precursor cells via incubating the purified

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subpopulation of cells in a FGF-containing medium configured for supporting adherent growth thereof ~~to obtain an isolated, purified population of rodent or human CNS neuron-restricted precursor cells~~ wherein said isolated pure population of neuron-restricted precursor cells differentiates into CNS neuronal cells upon replacement of adherent growth supporting medium with retinoic acid containing medium and wherein said isolated pure population of neuron-restricted precursor cells fails to proliferate or differentiate into CNS glial cells in astrocyte-promoting medium containing FGF and 10% fetal calf serum.

21. (Thrice amended) A method of isolating a pure population of rodent or human CNS neuron-restricted precursor cells comprising the steps of:

(a) removing a sample of spinal cord tissue from a rodent or human embryo at a stage of embryonic development after closure of the neural tube but prior to differentiation of glial and neuronal cells in the neural tube;

(b) dissociating cells comprising the sample of spinal cord tissue removed from the embryo;

(c) purifying from the dissociated cells a subpopulation expressing embryonic neural cell adhesion molecule;

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(d) plating the purified subpopulation of cells in feeder-cell-independent culture on a substratum and in a medium configured for supporting adherent growth of the neuron-restricted precursor cells; and

(e) isolating a pure population of rodent or human CNS neuron-restricted precursor cells via incubating the plated cells at a temperature and in an atmosphere conducive to growth ~~to obtain an isolated, pure population of neuron-restricted precursor cells~~ wherein said isolated pure population of neuron-restricted precursor cells requires FGF for adherent growth, differentiates into CNS neuronal cells upon replacement of adherent growth supporting medium with retinoic acid containing medium and fails to proliferate or differentiate into CNS glial cells in astrocyte-promoting medium containing FGF and 10% fetal calf serum.

59. (Twice amended) A method of isolating a pure population of mouse ~~or human~~ CNS neuron-restricted precursor cells comprising the steps of:

(a) providing a sample of mouse ~~or human~~ embryonic stem cells;



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(b) purifying from the mouse ~~or human~~ embryonic stem cells a subpopulation expressing embryonic neural cell adhesion molecule;

(c) plating the purified subpopulation of cells in feeder-cell-independent culture on a substratum and in a medium configured for supporting adherent growth of the neuron-restricted precursor cells; and

(d) isolating a pure population of mouse CNS neuron-restricted precursor cells via incubating the plated cells at a temperature and in an atmosphere conducive to growth of the neuron-restricted precursor cells wherein said isolated pure population of neuron-restricted precursor cells requires FGF and differentiates into CNS neuronal cells but not into CNS glial cells.